

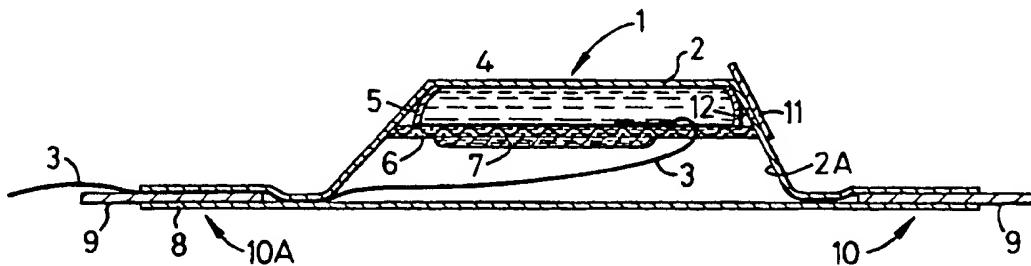


M12070

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁶ : A61M 35/00		A1	(11) International Publication Number: WO 97/04831 (43) International Publication Date: 13 February 1997 (13.02.97)
(21) International Application Number:	PCT/GB96/01856	(81) Designated States:	AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, ARIPO patent (KE, LS, MW, SD, SZ, UG), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).
(22) International Filing Date:	30 July 1996 (30.07.96)		
(30) Priority Data:	9515807.7 2 August 1995 (02.08.95) GB		
(71)(72) Applicant and Inventor:	CANTWELL, Evelyn, Dyson [GB/GB]; 250 Hendon Way, London NW4 3NL (GB).		
(74) Agents:	STEBBING, Peter, John, Hunter et al.; Ablett & Stebbing, 45 Lancaster Mews, Lancaster Gate, London W2 3QQ (GB).	Published	<i>With international search report.</i>

(54) Title: OXYGEN BANDAGE



(57) Abstract

The invention provides a topical hyperbaric bandage (1) comprising a gas diffusion resistant flexible and/or resistant sheet material (2) including an adhesive layer adapted to be affixed to the skin, said adhesive layer adapted to surround a treatment area, at least one release layer (7) disposed over said adhesive layer, and means for the supply of therapeutic gas to the treatment area, said device being adapted to retain a single charge of therapeutic gas over a treatment period; characterized in that said bandage (1) comprises a reservoir (4) for a source of therapeutic gas in liquid form, and in that gas from the reservoir is initiable (3) after the bandage has been secured to the skin.

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AM	Armenia	GB	United Kingdom	MW	Malawi
AT	Austria	GE	Georgia	MX	Mexico
AU	Australia	GN	Guinea	NE	Niger
BB	Barbados	GR	Greece	NL	Netherlands
BE	Belgium	HU	Hungary	NO	Norway
BF	Burkina Faso	IE	Ireland	NZ	New Zealand
BG	Bulgaria	IT	Italy	PL	Poland
BJ	Benin	JP	Japan	PT	Portugal
BR	Brazil	KE	Kenya	RO	Romania
BY	Belarus	KG	Kyrgyzstan	RU	Russian Federation
CA	Canada	KP	Democratic People's Republic of Korea	SD	Sudan
CF	Central African Republic	KR	Republic of Korea	SE	Sweden
CG	Congo	KZ	Kazakhstan	SG	Singapore
CH	Switzerland	LI	Liechtenstein	SI	Slovenia
CI	Côte d'Ivoire	LK	Sri Lanka	SK	Slovakia
CM	Cameroon	LR	Liberia	SN	Senegal
CN	China	LT	Lithuania	SZ	Swaziland
CS	Czechoslovakia	LU	Luxembourg	TD	Chad
CZ	Czech Republic	LV	Latvia	TG	Togo
DE	Germany	MC	Monaco	TJ	Tajikistan
DK	Denmark	MD	Republic of Moldova	TT	Trinidad and Tobago
EE	Estonia	MG	Madagascar	UA	Ukraine
ES	Spain	ML	Mali	UG	Uganda
FI	Finland	MN	Mongolia	US	United States of America
FR	France	MR	Mauritania	UZ	Uzbekistan
GA	Gabon			VN	Viet Nam

- 1 -

OXYGEN BANDAGE

The present invention relates to a topical hyperbaric bandage and to a method of wound healing utilising the same.

5

Hyperbaric apparatus for the treatment of open wounds and lesions by application thereto for therapeutic gas such as oxygen with or without a pharmacologically acceptable additive is generally known. For example in US-A-515 469 7 and 10 US-A-480 129 1 there are described various arrangements for the treatment of open lesions in wounds in a hyperbaric chamber with oxygen which promotes granulation, raises capillary blood oxygen levels and elevates redox potential thereby suppressing bacterial growth and encouraging 15 revascularisation.

In my earlier patent Application, WO94/21323 I have described a topical hyperbaric bandage comprising a gas diffusion resistant flexible and/or resilient sheet material including 20 an adhesive layer to be fixed to the skin, said adhesive layer surrounding the treatment area, at least one release layer disposed over the adhesive layer and means for supplying a therapeutic gas to the treatment area, the device being adapted to retain a single charge of a therapeutic gas over 25 a treatment period. The device may be further adapted such that it is rechargeable at least once with therapeutic gas for a repeat treatment whilst the device is in situ.

The advantage of arrangements of this type is that since 30 previously hyperbaric treatment was only available in suitably equipped hospitals, the arrangement according to my earlier application allowed the translation of hyperbaric treatment to the domestic sphere. This is because not only were the hyperbaric devices small, but also the oxygen supply required 35 was much smaller than had hitherto been the case.

- 2 -

Hyperbaric oxygen treatment has been somewhat controversial in the past because of the problems with oxygen toxæmia. We have found that relatively small super-atmospheric pressures of for example 1.03 to 1.04 atmospheres are 5 effective to assist in revascularisation as long as the treatment does not go on too long. For example, treatments of many conditions, eg. bedsores, for much longer than four hours at one time may well induce oxygen toxæmia and hence be counterproductive. Our previous invention was based on the 10 proposition that only a single charge of oxygen was not only necessary but highly desirable. Although, the single charge may be repeated after a few days or even after a few hours if required. The previous practice of flowing oxygen over a lesion for an indeterminate period was not only unnecessary, 15 but clinically counterproductive.

One attempt at producing such a bandage is to be found in GB-A-2024012. This reveals a two-part storable topical hyperbaric wound dressing which comprises a peroxy compound 20 such as hydrogen peroxide and an agent for activating the same to produce oxygen. Both components are absorbed or disposed on juxtaposed sheets and rely on either moisture from the wound to achieve activation or from the crushing of microspheres of the initiator prior to assembly about the 25 wound.

This arrangement is not satisfactory in part because the peroxy compounds are so labile when not liquid. Although they may be absorbed on a particular material experimentally, 30 storage in commercial conditions results in the peroxy compound deteriorating rapidly. This is particularly so at higher temperatures.

What is required therefore is a hyperbaric bandage which is 35 ready to use, easy to store and reliable. This is achieved in part by providing a liquid reservoir of the peroxy compound. A catalyst may not be required as such because

- 3 -

haemoglobin from the wound may act as the necessary catalyst in some circumstances.

The present invention is characterised in that the topical 5 hyperbaric bandage comprises a reservoir for a source of therapeutic gas in liquid form and in that gas release from the reservoir is initiable after the bandage has been secured to the skin. It will be appreciated that the therapeutic gas in non-gaseous form is most usually stored in chemical form 10 and is released by a biologically acceptable reaction which occurs within the device on actuation.

Thus the hyperbaric bandage may comprise a biologically acceptable means for a support of a reducing metal or other 15 catalyst or other reactive material, physically separated from the store but juxtaposed thereto. The therapeutic gas is usually mainly oxygen, the biologically acceptable support is most preferably an antiseptic pad secured or free within the bandage adjacent the proposed treatment area. The catalyst 20 may include compounds containing transition metals.

The source of therapeutic gas is preferably antiseptic itself in its stored form and is hyperbaric on release to the treatment area. One example of a therapeutic gas of this type 25 is oxygen emanating from the reaction of hydrogen peroxide, catalysed by a reducing metal catalyst such as zinc or copper or indeed, any other biologically acceptable reducing metal catalyst. Alternatively, the catalyst may be haemoglobin itself which it is to be found in fresh wounds. In which 30 case, either no separate catalyst is required, or such catalyst that is required is for secondary or back-up use.

The reservoir may comprise release means operable after the bandage is secured to the skin to provide communication 35 between the reservoir and the treatment area enclosed by the secured bandage; the establishment of communication serving to initiate the release of hyperbaric gas. One such means is

- 4 -

a drawstring moulded integrally with a store or reservoir such that it will open the reservoir to release a fluid into the treatment area to initiate gas generation. Alternatively, an adhesively attached aluminium foil can be employed. It will
5 be appreciated that the remote end of the drawstring or foil may be secured between the release layer and the adhesive layer prior to the securing of the bandage to the skin, and that a firm pull on the remote end of the drawstring will have the effect of ripping open or otherwise puncturing the
10 reservoir to release a liquid peroxy compound such as hydrogen-peroxide or percarbonate, stabilized if necessary, so that the liquid flows into contact with a zinc or copper catalyst deposited on a gauze to produce both free oxygen and water.

15

In a particularly preferred form of the invention the dressing or gauze may comprise a pharmaceutically acceptable humectant, for example TPH hydrophilic polymer (trade name), to bind water molecules on generation. The TPH hydrophilic polymer
20 belongs to a family of hydrophilic polyether polyurethanes and is particularly suited to this application because of its hydrophilic and gas permeable properties. The TPH hydrophilic polymer can be further used for a two part bandage whereby the TPH polymer dressing is adapted to remain in situ when the
25 rest of the bandage is removed. When a repeat hyperbaric treatment is required, a new hyperbaric bandage, but without a dressing, can be placed directly on top of the TPH polymer dressing without disturbing the wound.

30

Also, the TPH polymer may be impregnated with an appropriate anti-bacterial such that it can act as a bandage in-itself once it is separated from the hyperbaric device, and a normal surgical dressing is no longer required. Other matrices with
35 the properties of gas permeability and/or hydrophilicity may also be used in a similar fashion.

- 5 -

The hyperbaric bandage may be adapted to be rechargeable with a source of therapeutic gas on at least one occasion. In a preferred embodiment, there is provided an air-tight resealable vent on the upper surface of the bandage. A fresh 5 supply of for example hydrogen peroxide can be injected through the vent directly onto the dressing comprising the catalyst. Upon contact with the catalyst the therapeutic oxygen is released into the wound.

10 The therapeutic gas such as oxygen supplied to the treatment area may be heated to a temperature between 20°C and 44°C, preferably between 32°C and 39°C and more preferably about 37°C. This heating may be conveniently achieved by arranging that the peroxy-compound catalysis is exothermic. In such an 15 arrangement, the gas diffusion resistant material may be double walled, as in bubble film, to retain heat as far as possible.

20 The present invention will now be described by way of illustration only with reference to the accompanying drawings wherein:-

Figure 1 shows a vertical cross-section through a device of the invention.

25

Figure 2 shows a vertical cross-section through a device of the invention comprising a resealable vent.

With reference to Figure 1 a topical hyperbaric bandage (1) 30 is provided with a gas-impermeable flexible and/or resilient material (2) which is preferably a transparent plastics material such as a polyalkylene, polythene or PVC sheet in the general form of a rectangle or square having a dimension of for example 100mm by 120mm. The sheet material may be formed 35 by non-elastic stretching or thermo-forming with a pocket over the treatment area to retain a dressing therein, or merely to provide a greater area of containment of therapeutic gas.

- 6 -

The sheet material (2) is formed over the entirety of its lower surface with a first adhesive layer (2A) whereas the upper layer is essentially non-adhesive. The first adhesive layer (2A) is a thin hydrocolloid adhesive having a thickness 5 preferable of 0.45mm. Other suitable materials for adhering bandages for wound dressings etc. may be used with a thickness ranging between 0.20-0.60 mm.

Centrally disposed on the underside of the sheet material (2) 10 is a gas/liquid-impermeable reservoir material (5) containing a liquid chemical reservoir of releasable therapeutic oxygen such as hydrogen peroxide (4). Other chemically stored forms of releasable therapeutic oxygen may also be used. The reservoir (5) is made of resilient and/or flexible plastics 15 material and is adhered to the underside of the sheet material (2) with the adhesive layer (2A).

Juxtaposed below the reservoir (5), and preferably extending over the operative area is a gauze or dressing (6) of a 20 pharmacologically acceptable foamed material impregnated with a catalyst or reaction activator such as a transition metal compound. The dressing (6) may alternatively be a traditional multi-layer woven material. The dressing (6) extends beyond the periphery of the reservoir (5) such that its exposed upper 25 surface is fixedly adhered to the underside of the sheet material (2) with the adhesive layer (2A). Alternatively the dressing may be omitted along with the catalyst or reaction activator since haemoglobin from the wound will act as a catalyst for the peroxy compounds.

30 Integral with the reservoir material (5) there is a release means (3), preferably a strong string, the first end of said string or foil (3) being detachably attached to the reservoir material (5) along a line of weakness such that when the 35 string (3) is pulled, the reservoir material (5) tears to release the hydrogen peroxide (4) onto the dressing (6). The string (3) is threaded through or over the dressing (6) and

- 7 -

then between the adhesive layer (2A) of the sheet material (2) and a secondary release layer (9) (described below) such that an adequate portion of the string (3) extends beyond the secondary release layer (9) to leave the second end of the
5 string (3) a free end. Alternative release means may also be used such that the air-tight seal over the operative area is not compromised such as aluminium foil disposed over a preformed aperture.

10 To the underside of the edges of the sheet material (2) is applied a primary release layer (8) which is secured to the adhesive layer (2A) on the underside of the sheet material (2), and generally conforms to the exterior periphery thereof. The release layer is an essentially non-adhesive layer which
15 forms a weak bond with the adhesive layer (2A) disposed on the underside of the sheet material (2). In the arrangement shown in Figure 1 the release layer is formed in a two layer partially overlapped configuration, whereby the removal of the primary release layer (8) allows a portion of the adhesive
20 face to be exposed for contact with the skin about the wound. A secondary release layer (9) is secured to each parallel side of the sheet material (2). This arrangement allows the device to be correctly orientated relative to the wound and secured in this orientation while the second release layer (9) or
25 layers are removed so that the device is correctly orientated on the skin without folds or rucks. In the arrangement as shown in Figure 1 the edge portions of the primary release layer (8) do not adhere to the underside of the sheet material (2) but are left free. The secondary release layer (9),
30 however, is adhered to the remaining underside on each parallel side of the sheet material (2) in between the primary release layer (8) and the sheet material (2).

35 Optionally, the dressing (6) may further comprise a layer of humectant or inert hygroscopic material (7) on the side not in contact with the reservoir (5). This enables any residual water resulting from a chemical reaction to be absorbed and

- 8 -

allows the wound area to remain dry. Whether the addition of the hygroscopic material (7) is required will be determined by the type of reaction used to release the therapeutic gas from a stored form.

5

In an alternative arrangement the topical hyperbaric bandage (1) may be in two parts such that the sheet material (2) can be removed after hyperbaric treatment of the wound area whilst the dressing (6) is left in situ. Thus the lesion is not 10 disturbed during repeated treatments. The dressing may be impregnated with an appropriate anti-bacterial composition to prevent the lesion from becoming infected or septic. When the next hyperbaric treatment is required, a new bandage (1) but without the dressing (6) can be applied directly on to the 15 dressing (6) from the previous treatment. The dressing (6) for use in this manner is suitable for several repeat treatments. Specifically, the dressing in this embodiment is a hydrophilic polymer which belongs to a family of hydrophilic polyether polyurethanes and is currently marketed under the 20 trade name TPH hydrophilic polymer. The TPH polymer is a gas permeable matrix and is also hydrophilic. These properties are particularly suited for this invention, since the TPH polymer can absorb the water released from the hydrogen peroxide reaction and since the polymer is gas permeable, the 25 hyperbaric treatment is unhindered.

With reference to Figure 2, in an alternative arrangement of a hyperbaric bandage there may be a resealable vent (12) on the upper surface of the sheet material (2). The air-tight 30 seal is achieved with for example a second layer of adhesive sheet material (11). The vent allows access to the dressing (6) and the space therebelow only. Thus, when a repeat hyperbaric treatment is required, the second layer of sheet material (11) is removed and a given quantity of hydrogen 35 peroxide injected onto the dressing. The second layer of sheet material (11) is replaced immediately to reseal the vent (12) and prevent escape of evolved oxygen. The fresh hydrogen

- 9 -

peroxide reacts with the catalyst in the dressing (6) to evolve the therapeutic oxygen.

Further, during application of the bandage to the skin, the
5 vent (12) may be opened and the raised portion of the bandage compressed against the skin to expel as much air as possible, prior to the release of the hydrogen peroxide, thereby to allow the space between the dressing (6) and the lesion to fill with a greater proportion of released oxygen.

10

The hyperbaric device (1) is applied to a preferably dirt and grim free, smoothed or pre-shaven skin. The first underside (10) of the hyperbaric device (1) is the side not comprising the free end of the string (3) whereas the second underside 15 (10A) of the hyperbaric device (1) comprises the free end of the string (3). The said first underside (10) is fixed onto the pre-treated skin first by peeling off both the first release layer (8) and the second release layer (9). Then whilst firmly pressing the sheet material (2) on the second 20 underside (10A) onto the skin, the remaining secondary release layer (9) is peeled off. Once the hyperbaric device (1) is thus securely in position the free end of the string (3) can be pulled out firmly from the second underside (10A) which forms an air-tight seal between the sheet material (2) and the 25 skin.

Upon thus pulling the string (3) the reservoir (5) tears to release the hydrogen peroxide (4) onto the catalyst impregnated in the dressing (6). The ensuing chemical 30 reaction between the hydrogen peroxide and the reducing metal catalyst, releases a charge of oxygen over a period of about 5 to 20 minutes. The released oxygen is trapped within the gas-impermeable sheet material (2) and thereby creates a small super-atmospheric pressure of around 1.03 to 1.04 atmospheres 35 thereby being brought into contact with the wound. The water resulting from such a chemical reaction may be absorbed into the inert hygroscopic material (7).

- 10 -

The quantity of hydrogen peroxide in the reservoir is determined by the amount of oxygen required to effectively treat a given lesion. For example 1 ml of 2M H₂O₂ will release sufficient oxygen to create a pressure of around 2.20 atmospheres within the enclosed device where the dimensions of the enclosed volume are 5 cm by 2 cm by 1 cm deep. However, it is estimated that since at least 40% to 60% of the released oxygen will be lost through seepage, absorption into surrounding materials, incomplete reaction and natural diffusion, there will be a working pressure of at least 1.03 atmospheres which is more than sufficient to allow a charge of oxygen to enter the wound.

15 By suitable adjustment of the quantities of hydrogen peroxide in relation to the volume of enclosed area between the wound and the device (1) when fixed in position, the problem of hypoxia and over inflation of the hyperbaric device (1) is avoided.

20

Devices in accordance with the present invention may thus be applied such as to reduce hypoxia but avoid oxygen toxæmia. Typical regimes such as one treatment of 20 minutes to 2 hours duration twice a day to repeated treatments over several days allow wounds and lesions to cure quickly.

Each device is for a single use and is disposable after one use. Optionally, in a second embodiment, there may be a facility for injecting a given quantity of fresh hydrogen peroxide into the device, to recommence the reaction.

35 It will be appreciated that because of the portable nature of the device and the ease of use, patients with lesions can apply the device to the wound themselves without the need for

- 11 -

professional medical intervention. Accordingly, the arrangement of the present invention is cheap and easy enough to use to bring hyperbaric treatment more widely into use.

- 5 The invention provides, therefore a topical hyperbaric device for a single application; a disposable device comprising a self-contained liquid store of therapeutic gas such as oxygen, said gas being released into the wound upon chemical activation by a catalyst or by the catalytic action of
10 haemoglobin.

- 12 -

CLAIMS

1. A topical hyperbaric bandage comprising a gas diffusion
resistant flexible and/or resistant sheet material including
5 an adhesive layer adapted to be affixed to the skin, said
adhesive layer adapted to surround a treatment area, at least
one release layer disposed over said adhesive layer, and means
for the supply of therapeutic gas to the treatment area, said
device being adapted to retain a single charge of therapeutic
10 gas over a treatment period;

characterised in that said bandage comprises a reservoir for
a source of therapeutic gas in liquid form, and in that gas
release from the reservoir is initiable after the bandage has
15 been secured to the skin.

2. A bandage according to claim 1 wherein the bandage
comprises a biologically acceptable means for the support of
a compatible reducing metal catalyst, physically separated
20 from the reservoir but juxtaposed there to.

3. A bandage according to claim 2 wherein the therapeutic
gas is mainly oxygen and wherein the biologically acceptable
support is an antiseptic gauze or pad within the bandage.
25

4. A bandage according to claim 3 wherein the source of
therapeutic gas is antiseptic in its stored form and
hyperbaric on its release.

30 5. A bandage according to claim 4 wherein the source of
therapeutic gas is peroxy compound and the catalyst is a
biologically acceptable reducing metal.

35 6. A bandage according to any preceding claim where the
reservoir comprises release means operable as or when the
bandage has been secured to the skin to provide communication

- 13 -

to the store and the treatment area enclosed by the second secured bandage, the establishment of communication serving to initiate the release of hyperbaric gas.

5 7. A bandage according to claim 6 wherein the release means is a drawstring adapted to open a reservoir to release a fluid into the treatment area to initiate gas generation.

8. A bandage according to claims 3 to 7 wherein the gauze
10 or pad comprises a pharmacologically acceptable humectant to bind water molecules on generation.

9. A bandage according to any preceding claim wherein the dressing is adapted to remain in situ when the rest of the
15 bandage is removed.

10. A bandage according to any preceding claim wherein the dressing is a hydrophilic polyether polyurethane.

20 11. A bandage according to any preceding claim wherein the bandage is adapted to be rechargeable with a source of a therapeutic gas for repeat treatments.

12. A bandage according to claim 11 comprising a resealable
25 vent.

1/1

FIG. 1

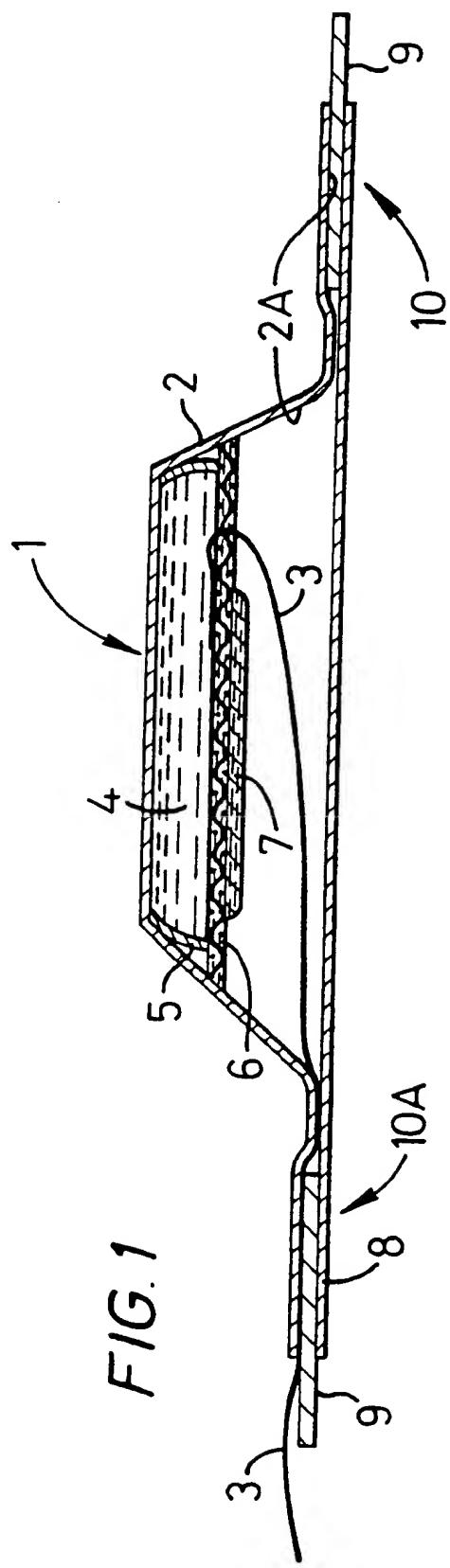
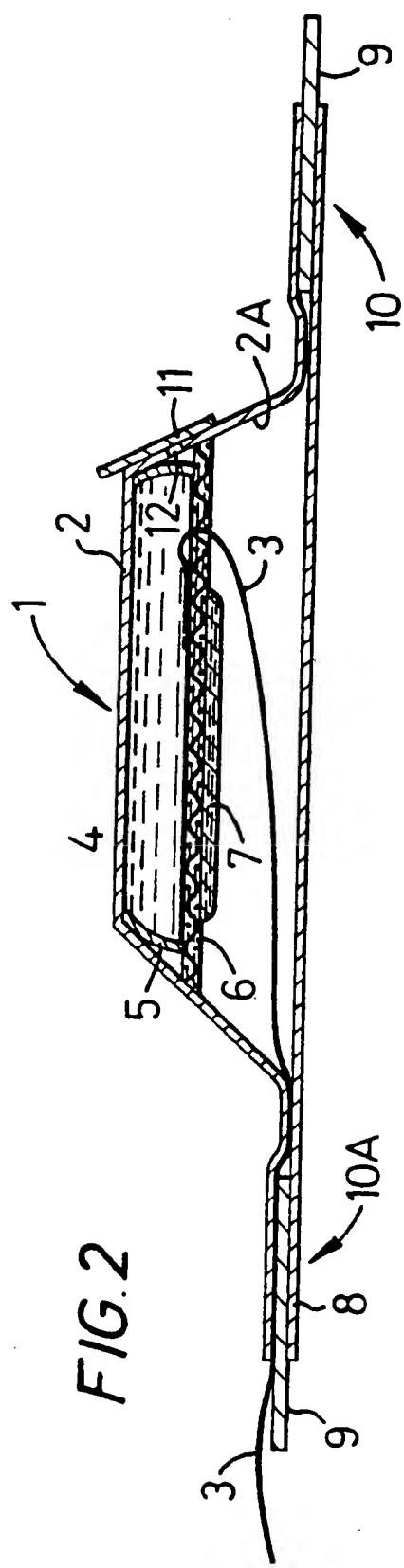


FIG. 2



INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 96/01856

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 A61M35/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 A61M A61L

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	GB,A,2 024 012 (JOHNSON & JOHNSON) 9 January 1980 cited in the application * The Whole Document * ---	1-12
Y	US,A,5 128 137 (MÜLLER ET AL.) 7 July 1992 see abstract see column 1, line 24 - column 2, line 20; claims 2-5; figures 1-3 ---	1-12
A	WO,A,90 00416 (ALZA CORPORATION) 25 January 1990 -----	

 Further documents are listed in the continuation of box C. Patent family members are listed in annex.

* Special categories of cited documents :

- *'A' document defining the general state of the art which is not considered to be of particular relevance
- *'E' earlier document but published on or after the international filing date
- *'L' document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *'O' document referring to an oral disclosure, use, exhibition or other means
- *'P' document published prior to the international filing date but later than the priority date claimed

*'T' later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

*'X' document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

*'Y' document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

*'&' document member of the same patent family

Date of the actual completion of the international search

Date of mailing of the international search report

12 November 1996

14. 11. 96

Name and mailing address of the ISA
European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+ 31-70) 340-2040, Tx. 31 651 epo nl.
Fax (+ 31-70) 340-3016

Authorized officer

Michels, N

INTERNATIONAL SEARCH REPORT

Information on patent family members

Int'nal Application No

PCT/GB 96/01856

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
GB-A-2024012	09-01-80	NONE		
US-A-5128137	07-07-92	DE-A- 3903794 CA-A,C 2009558 DE-D- 59003039 EP-A- 0382129 ES-T- 2047171 IE-B- 64835 JP-A- 2264715 JP-B- 2538371		16-08-90 09-08-90 18-11-93 16-08-90 16-02-94 06-09-95 29-10-90 25-09-96
WO-A-9000416	25-01-90	US-A- 4917895 AU-A- 4038089 EP-A- 0380638 JP-T- 3500301		17-04-90 05-02-90 08-08-90 24-01-91